Appendix A: Sample Consent

Penn Medicine

Informed Consent Form and HIPAA Authorization

Protocol Title:	Transfusion of Prematures – Does a Liberal Red Blood Cell Transfusion Strategy Improve Neurologically-Intact Survival of Extremely-Low-Birth Weight Infants as Compared to a Restrictive Strategy
Short Title:	Transfusion of Prematures (TOP)
Principal Investigator:	Haresh Kirpalani, BM, MSc Division of Neonatology and Newborn Services Hospital of the University of Philadelphia 34th and Spruce Street Philadelphia, PA 19104 215-662-3228
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Thank you for taking time to read this when so much is happening to your baby. We know it is a difficult time for you.

Why am I being asked to have my baby participate in the study?
You and your baby are being invited to participate in a research study. Your baby's participation is voluntary meaning you can choose whether or not you want your baby to participate. If you choose not to have your baby participate, there will be no loss of benefits to which your baby is otherwise entitled. Before you can make your decision, you will need to know what the study is about and the possible risks and benefits of being in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You can also discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to have your baby participate, you will be asked to sign this form.

What is the purpose of this research study?
Doctors and nurses need to better understand when we should transfuse blood (as red cells) into the blood of premature infants. Blood contains red cells, which carry a molecule called hemoglobin.

Hemoglobin is essential for life as it carries oxygen around the body. Hemoglobin can be measured, and is used by doctors as a measure of how many red blood cells are circulating in your baby's body.

Because premature babies need intensive care, they need a lot of blood tests to monitor their care. Doctors try their best to order only a few blood tests depending on the needs of the premature babies. Since premature infants cannot make red blood cells easily, they sometimes become anemic. Therefore, we have to give them blood transfusions.

When the hemoglobin falls below a certain level, doctors will transfuse the baby. However, we know that some doctors tend to use a higher level of hemoglobin and some doctors tend to use a lower level of hemoglobin. The reason for this is that we do not know which level of hemoglobin is better. This study aims to help us find out when we should best transfuse babies.

This study has been designed to gather information to understand at which level of hemoglobin we should transfuse for the best results. This study has been approved and funded by the National Heart, Lung and Blood Institute and the Eunice Kennedy Shriver National Institute of Child Health and Human Development, branches of the National Institutes of Health and 18 large hospitals in the US are doing this study. Information about this study is available on a public registry website (http://clinicaltrials.gov/ Identifier: NCT 01702805)

How long will my baby be in the study? How many other babies will be in the study?

Your baby will remain in the study for the duration of his/her hospital admission and until the date of the 22-26 month follow-up appointment. The 22-26 month follow-up appointment will be conducted at any of the 3 CHOP affiliated Neonatal Follow-up clinics.

This study will enroll 1824 babies from across the country.

What does the study involve?

Babies like yours, who are born extremely premature and who need intensive care, require a lot of blood tests. Because they cannot form new blood cells as fast as they are being removed, very premature babies become anemic and often require blood transfusion. We know that 90% of babies like yours receive at least one blood transfusion during their stay in the intensive care unit.

Anemia is measured by the level of hemoglobin in the blood and blood transfusions are given when hemoglobin falls below a certain level. It is routine to receive blood transfusions at hemoglobin levels based on your doctor's choice. We have found that some doctors tend to use the higher levels and some doctors tend to use the lower levels. This is because at the moment, no one knows which level of hemoglobin is better.

The levels at which babies are being transfused in this study are well within the range at which doctors across the country routinely transfuse now, we are just establishing what is the best level.

This study is trying to provide an answer to the question: "What is the best level of hemoglobin for transfusing babies?". If you agree that your baby should take part in this study, your baby will be randomly assigned (like a flip of a coin) to either the higher level of hemoglobin or the lower level. Both

of these levels are in the usual range used by doctors in the NICU. The doctor will use this level of hemoglobin to decide when to transfuse the baby.

If your baby were to get unexpectedly ill or have an unexpected urgent need for blood transfusion (where everybody would routinely give blood), your baby would get the transfusion regardless of the level of hemoglobin.

All of the blood tests that are done are routine standard of care.

We will ask you to complete an economic questionnaire that will help provide us with information as to how families cope with having a baby in the intensive care nursery. We will ask you for information about additional expenses that you have related to your child's hospitalization and medical care following discharge. You are free to decline to answer some or all of these questions. If you decide that you do not want to complete the economic questionnaire, this will not affect study participation or the care that your baby receives in the hospital.

We will collect information from the hospital about daily financial charges for your child's medical care. This will not include any of your personal financial information or your social security number. This will help us determine the cost of taking care of premature babies today in the United States.

We will arrange for your baby to come back for a 22 month follow-up appointment. All extremely premature babies are routinely seen in the Follow-up clinic to check how well they develop and grow.

We will also observe how well your child has learnt to walk, talk and play. We will also ask you to complete a short questionnaire about how your life and work has been impacted by your baby's stay in the hospital.

What are the possible risks or discomforts?

Your baby has been born very early, and is at risk for complications of extreme prematurity, and some of these babies die. This study does not carry any additional risks to your baby if you choose to take part. There are no extra blood tests being done on your baby. All blood tests are done as routine standard of care at your doctor's request. This study does not alter the routine care for your baby. The risks associated with this study are exactly the same risks that exist in current medical practice and in blood transfusion therapy. If your baby needs blood for emergency reasons, where all doctors would routinely give blood, they will get the blood they need – irrespective of the study. After that urgent need is over, they will then return to the study protocol.

Blood transfusions are nowadays, in general extremely safe. It is simply that giving blood transfusions at too high a hemoglobin level may result not only in more blood transfusions, but the babies may take longer to mature their own bone marrow to produce their own blood. On the other hand, transfusing at too low a hemoglobin, could lead to the baby not having enough hemoglobin to carry enough oxygen around the body. We avoid these extremes by transfusing within the ranges of hemoglobin level that doctors nowadays already use.

During the entire study, an independent committee will review this study to make sure that it continues to be safe.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

This study may not directly benefit your baby. However, your baby may benefit from additional monitoring during the study.

What other choices do I have if I do not participate?

If you choose not to participate in this study and if your baby needs a blood transfusion, the doctor will decide at which level of hemoglobin to use in making the decision to transfuse your baby.

Will I be paid for being in this study?

You will not receive any payments for taking part in this study. However, if necessary, we will cover the cost of travel to the CHOP follow up clinic for the visit at 22 to 26 months.

Will I have to pay for anything?

While you are in this study, the cost of your medical care – procedures, medications and doctor visits – will continue to be billed to you or your insurance.

What happens if I am injured from being in the study?
If you are hurt or get sick from something that was done as part of this study, doctors at the clinic or hospital can arrange for emergency medical care. The Hospital does not offer financial compensation or payment for injuries due to participation in this research. No funds have been set aside to compensate you in the event of injury.
You and your insurance company will be billed for the costs of any care or injuries.
If you think you have been injured from taking part in this study, call Dr. Haresh Kirpalani at 215-590-3730. He can go over things with you, let you know of resources that may be available and give you information on what you need to do.
In case of injury resulting from this study, you will not lose any legal rights by signing this form.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed their 22 - 26 month neurodevelopmental assessment visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
You have not followed study instructions.

The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?
We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Your baby will be assigned a unique study ID number. There will be one Master List which will contain the name of your baby and the assigned study ID number. No one outside of the immediate study team will know the true identity of your baby. Once your baby has completed the 22 month follow-up visit, the link between the name and study ID number will be destroyed. Only the study ID number is used on all study data forms.

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record. Your baby will have an EMR since he/she is an inpatient in the Intensive Care Nursery of the University of Pennsylvania Health System.

If you choose to have your baby participate in this trial, documentation of this will be included in the EMR. This trial does not require any additional tests or procedures outside of routine intensive care.

Documentation that is entered in the EMR, is accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?
If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with Dr. Haresh Kirpalani listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

Parental Informed Consent Form

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.
A copy of this consent form will be given to you.

Name of Subject (Please Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date

For subjects unable to give authorization, the authorization is given by the following authorized subject representative:

Authorized subject representative [print]	Authorized subject representative Signature	Date

Provide a brief description of above person authority to serve as the subject's authorized representative.